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10/033,297	11/02/2001	Jeff G. Hall	FORS-06675	1030

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,297	HALL ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *35-51* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 April 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of species (10) filed on February 9, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Since applicant has elected Group I, claims 35-51 and species (1) (claim 37) and species (6) (claim 48) in the response filed on September 21, 2003, claims 35-37, 39-41, 43-48, and 51 will be examined.

Drawings

2. Some words in Figures 1A to 1H, 2A to 2C , 3, 4, 13, 14, 15A to 15E, 19, 20A, 23, 31, 32, 44, 45, 48, 54, 56, 59A to 59E, 69-72, 75A to 75C, 81, 84, and 97 are hard to read. The quality of Figures 61 and 80 is poor and there is no label "Figure 96" in the drawings. The replacement is required. No new matter will be introduced in the required drawing.

Information Disclosure Statement

3. Applicant notes that applicant filed IDS on September 12, 2003. However, the examiner cannot locate the references listed in Form PTO –1449 and these references have not been scanned and cannot be found in electric file (eDAN).

Specification

4. The disclosure is objected to because of the following informalities: (1) applicant cites several parent applications in the first sentence of the specification. However, it is unclear that applicant claims priority for these parent applications or not; (2) the specification (page 23) describes Figures 3A to 3G, 4A, 4B, 36A, and 36B. However, there is no Figures 3A to 3G, 4A, 4B, 36A, and 36B; and (3) there are Figures 1A to 1H, 2A to 2C, 42A, 42B, 59A to 59E, 88A, and 88B. However, the specification (see page 23) only describes Figures 1, 2, 42, 59, and 88.

Appropriate correction is required.

Claim Objections

5. Claim 35 is objected to because of the following informalities: " that can be, cleaved" should be " that can be cleaved".

Appropriate correction is required

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 35-37, 39-41, 43-48, and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To the extent that the claimed methods are not described in the instant disclosure, claims 35-37, 39-41, 43-48, and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Since, in applicant's remarks filed on November 2, 2001, applicant does not indicate which part in the specification supports newly added claims, 35-37, 39-41, 43-48, and 51, claims 35-37, 39-41, 43-48, and 51 are considered as new matter. Particularly, the specification fails to define or provide any disclosure to support for the phrases "a flap region", "a reporter precursor" and "the signal exhibits a specific behavior as a function of time" recited in claim 1, "wherein the specific behavior as a function of time is non-linear" as recited in claim 40, "wherein the specific behavior as a function of time is quadratic" as recited in claim 41, and "the determination of whether the signal exhibits a specific behavior as a function of time is performed in real time" recited in claim 48.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112,

FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 35-37, 39-41, 43-48, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 35 is rejected as vague and indefinite because it is unclear how step (c), "determining whether the signal exhibits a specific behavior as a function of time" correlates with the preamble "detecting a target polynucleotide" since there is no method step to detect a target polynucleotide. A method step correlating the detection of the target nucleic acid molecules with the specific behavior is required to overcome the rejection. Please clarify.

11. Claim 35 recites the limitation "the cleaved flap region" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no phrase "a cleaved flap region" in step (a). Please clarify.

12. Claim 35 is rejected as vague and indefinite in view of the phrase "the cleaved flap region of the probe oligonucleotide and the reagent can come into contact with a reporter precursor to which the flap region of the probe oligonucleotide is capable of hybridizing to form a complex that can be, cleaved by the reagent to provide a reporter capable of being detected" because, if a complex formed by the flap region of the probe oligonucleotide and a reporter precursor can be cleaved by the reagent, how the flap region of the probe oligonucleotide and a reporter precursor

can form a complex in the presence of the reagent. Therefore, the first part of the phrase and the second part of the phrase do not correspond each other. Please clarify.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 35-37, 43-45, and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodman *et al.*, (US Patent No. 4,994,368, published on February 19, 1991).

Goodman *et al.*, teach amplification method for polynucleotide assays.

Regarding claims 35 and 47, Goodman *et al.*, teach a method of producing multiple copies of a primary polynucleotide sequence as the result of the presence of a target polynucleotide sequence located at the 3' terminus of a polynucleotide, which comprises: (a) forming in the presence of nucleoside triphosphates and template-dependent polynucleotide polymerase an extension of a target polynucleotide sequence hybridized with a binding polynucleotide sequence of a single stranded pattern polynucleotide comprising said binding polynucleotide sequence and two or more copies of a template sequence each containing one or more site specific cleavage sequences; (b) cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences; (c) dissociating said fragments, wherein said fragments comprise said primary

polynucleotide sequence; (d) hybridizing said fragments with said single stranded pattern polynucleotide; (e) forming in the presence of said nucleoside triphosphates and said template dependent polynucleotide polymerase an extension of said fragments hybridized with said single stranded pattern polynucleotide; and (f) repeating steps (b)-(e) above wherein steps (b)-(e) are conducted simultaneously or wholly or partially sequentially (see claim 18, column 30 and Figures 1-4). Since Goodman *et al.*, teach forming in the presence of nucleoside triphosphates and template-dependent polynucleotide polymerase an extension of a target polynucleotide sequence hybridized with a binding polynucleotide sequence of a single stranded pattern polynucleotide comprising said binding polynucleotide sequence and two or more copies of a template sequence each containing one or more site specific cleavage sequences and cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences (see above), Goodman *et al.*, disclose contacting a target polynucleotide (ie., target polynucleotide sequence taught by Goodman *et al.*,) having a first portion and a second portion immediately contiguous to one another with: i) an invader oligonucleotide (i.e., one site specific cleavage sequence), at least a part of which is capable of specifically hybridizing to the first portion of the target polynucleotide; ii) a probe oligonucleotide (i.e., another site specific cleavage sequence) comprising a first region that is capable of specifically hybridizing to the second portion of the target polynucleotide and a flap region located adjacent to the first region; and iii) a reagent that is capable of cleaving the flap region of the probe oligonucleotide (i.e, means for specifically cleaving said cleavable polynucleotide sequences) when the probe oligonucleotide is hybridized to the second portion of

the target polynucleotide and the invader oligonucleotide is hybridized to the first portion of the polynucleotide as recited in claim 35. Since Goodman *et al.*, teach cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences, dissociating said fragments wherein said fragments comprise said primary polynucleotide sequence, hybridizing said fragments with said single stranded pattern polynucleotide, forming in the presence of said nucleoside triphosphates and said template dependent polynucleotide polymerase an extension of said fragments hybridized with said single stranded pattern polynucleotide, and repeating steps (b)-(e) above wherein steps (b)-(e) are conducted simultaneously or wholly or partially sequentially (see above) wherein said fragments are labeled with a fluorescence after cleavage (see claims 11-17 in claims 29 and 30), Goodman *et al.*, disclose under conditions such that the cleaved flap region of the probe oligonucleotide (i.e., cleaved fragments taught by Goodman *et al.*,) and the reagent (i.e, means for specifically cleaving said cleavable polynucleotide sequences) can come into contact with a reporter precursor (ie., said single stranded pattern polynucleotide) to which the flap region of the probe oligonucleotide is capable of hybridizing to form a complex (i.e., a complex formed by said fragement and said single stranded pattern polynucleotide) that can be cleaved by the reagent to provide a reporter (i.e., said fragments labeled with a fluorescence) capable of being detected as recited in claim 35. Since the cleaved fragments taught by Goodman *et al.*, are detected by their fluorescent signals (see column 19, second paragraph), Goodman *et al.*, disclose detecting the reporter (ie., said fragments labeled with a fluorescence) to provide a signal as recited in step (b) of claim 35. Since Goodman *et al.*, teach repeating steps (b)-(e) (see

above), Goodman *et al.*, must teach repeat detection of said fragments labeled with a fluorescence in different time periods. Since said fragments labeled with a fluorescence may have a slight difference in their fluorescent signal and there is no definition for "a specific behavior as a function of time" in the specification, Goodman *et al.*, disclose determining whether the signal exhibits a specific behavior (slight increase or decrease in fluorescent signal) as a function of time (ie., different time periods) as step (c) of claim 35 and claim 47.

Regarding claims 36 and 37, since Goodman *et al.*, teach forming in the presence of nucleoside triphosphates and template-dependent polynucleotide polymerase an extension of a target polynucleotide sequence hybridized with a binding polynucleotide sequence of a single stranded pattern polynucleotide comprising said binding polynucleotide sequence and two or more copies of a template sequence each containing one or more site specific cleavage sequences (see claim 18 in column 30), Goodman *et al.*, disclose that the invader oligonucleotide (ie., one site specific cleavage sequence) comprises a first region (ie., part of one site specific cleavage sequence) that is capable of specifically hybridizing to the first portion of the target polynucleotide, and a flap region (ie., part of one site specific cleavage sequence) located adjacent to the first region as recited in claim 36 and the flap region of the invader oligonucleotide is capable of specifically hybridizing to the target polynucleotide as recited in claim 37.

Regarding claims 43-45, since, the first region and the flap region of the invader oligonucleotide can be located at either 5' or 3' of one site specific cleavage sequence taught by Goodman *et al.*, and the first region and the flap region of the probe can be either 5' or 3' of another site specific cleavage sequence taught by Goodman *et al.*, Goodman *et al.*, disclose that

the flap region of the invader oligonucleotide is located immediately 3' to the first region of the invader oligonucleotide, and the flap region of the probe (ie., another site specific cleavage sequence) is located immediately 5' to the first region of the probe recited in claims 43-45 wherein the invader oligonucleotide and the probe are one site specific cleavage sequence and another site specific cleavage sequence taught by Goodman *et al.*.

Regarding claim 51, since the target polynucleotide sequence taught by Goodman *et al.*, has a first portion (ie., 3' part of the target polynucleotide sequence taught by Goodman *et al.*,) and a second portion (ie., 5' part of the target polynucleotide sequence taught by Goodman *et al.*,), Goodman *et al.*, disclose that the second portion of the target polynucleotide is located immediately 5' to the first portion of the target polynucleotide as recited in claim 51.

Therefore, Goodman *et al.*, teach all limitations recited in claims 35-37, 43-45, and 51.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 39 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman *et al.*, as applied to claims 35-37, 43-45, and 51 above, and further in view of McKenzie (US Patent No. 5,401,830, published on march 28, 1995).

The teachings of Goodman *et al.*, have been summarized previously, *supra.*

Regarding claim 46, since claim 46 is identical to claims 43-45, Goodman *et al.*, teach claim 46.

Goodman *et al.*, also teach that their method is used in polynucleotide analytes from any source (see column 5 and Table 1).

Goodman *et al.*, do not disclose that the flap region of the invader oligonucleotide comprises a first section that is not capable of specifically hybridizing to the target polynucleotide (ie., a mutation in the flap region of the invader oligonucleotide) and a second section that is capable of specifically hybridizing to the target polynucleotide as recited in claim 39.

McKenzie teaches that mutations in a sample are selected by preferential hybridization of an oligonucleotide containing the mutation (see column 15, Example 7).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 36 using a invader oligonucleotide with a mutation in the flap region of the invader oligonucleotide (a first section that is not capable of specifically hybridizing to the target polynucleotide) in order to detect suspected mutations in a sample containing polynucleotide analytes in view of the patents

of Goodman *et al.*, and McKenzie. One having ordinary skill in the art would have been motivated to do so because McKenzie suggests that mutations in a sample containing polynucleotide analytes are selected by preferential hybridization of an oligonucleotide containing the mutation (see column 15, Example 7). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claim 36 using a invader oligonucleotide with a mutation in the flap region of the invader oligonucleotide in order to detect suspected mutations in a sample containing polynucleotide analytes.

Conclusion

17. No claim is allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
April 16, 2004

FRANK LU
PATENT EXAMINER